immobilized cell culture, and/or at a position of increased concentration of a certain component of the medium of interest.

While such orientation may be beneficial for determining local concentrations of specific analytes at a predetermined position, it is often desirable to agitate the medium of interest, e.g. in order to provide a homogeneous distribution of the components throughout the medium. However, it has been found that agitation (e.g. stirring) of the medium surrounding the microdialysis probe leads to disadvantages. On the one hand, large particles and/or debris present in the medium of interest may collide with the probe due to agitation, which can cause damage to the semipermeable membrane. On the other hand, the positioning of the probe in the medium of interest as known in the art affects the fluid dynamics of the agitated medium inside the reactor, causing undesired turbulences in the medium of interest. These turbulences can lead to increased shear stress both on the semipermeable membrane of the probe and on potentially sensitive components of the medium of interest, and increase the risk of mechanically damaging both the probe and the potentially sensitive components of the medium.

US 2007/0292958 relates to apparatuses and methods for analyzing enzyme reactions, including large, industrial-scale reactions. The method involves the use of microdialysis probes connected to an analytic device, e.g. for HPLC analysis, introduced into stirred reactors. To protect the probe from damage, by collision with large particles or debris, an outer sleeve made from polypropylene mesh can be provided around the probe. However, while such a sleeve protects the probe from collisions, the disadvantages arising from altered fluid dynamics of the agitated medium are not addressed.

It now has been surprisingly found that the effects of the probe on the fluid dynamics of an agitated medium, and the disadvantages associated therewith, can be substantially reduced or eliminated by selection of a specific shape, orientation and/or position of the probe within a reactor.

Summary

One aspect of the present disclosure is an apparatus comprising a reactor, preferably a bioreactor; and at least one probe comprising a first surface and a second surface and at least one hollow conduit for transporting fluids, formed between the first surface and the second surface, running along the first surface and the second surface, wherein the hollow conduit has an inlet opening for receiving fluids, and an outlet opening for releasing fluids received through the inlet opening and transported through the hollow conduit, wherein the first surface is made at least partially from a semipermeable membrane, and the semipermeable membrane forms a wall of a

semipermeable portion of the hollow conduit, and wherein the first surface is exposed to the interior volume of the reactor, and wherein the probe is fixed permanently or non-permanently to a portion of an inner surface of a wall of the reactor with the second surface of the probe facing the portion to which the probe is fixed.

Another aspect of the disclosure is a kit of components comprising the reactor and probe as defined above, and optionally at least one fluid source and/or at least one instrument for collecting and/or analyzing fluids, wherein the probe is configured to be fixed permanently or non-permanently to a portion of an inner surface of a wall of the reactor with the second surface of the probe facing the portion to which the probe is fixed.

A further example of the disclosure is a probe comprising a first surface and a second surface and a hollow conduit for transporting fluids, formed between the first surface and the second surface, running along the first surface and the second surface, wherein the hollow conduit has an inlet opening for receiving fluids, and an outlet opening for releasing fluids received through the inlet opening and transported through the hollow conduit, wherein the first surface is made at least partially from a semipermeable membrane, and the semipermeable membrane forms a wall of a semipermeable portion of the hollow conduit, and wherein the first surface and the second surface of the probe deviate from being planar, and the curvatures of the first surface and the second surface of the probe are essentially concentric, and wherein the probe is configured to be fixed permanently or non-permanently to a portion of an inner surface of a wall of a reactor with the second surface of the probe facing the portion to which the probe is configured to be fixed.

Thus, there is provided in one aspect a probe (100) comprising a first surface (150) and a second surface (160) and a hollow conduit (110) for transporting fluids, formed between the first surface (150) and the second surface (160), running along the first surface (150) and the second surface (160), wherein the hollow conduit (110) has an inlet opening (120) for receiving fluids, and an outlet opening (130) for releasing fluids received through the inlet opening (120) and transported through the hollow conduit (110),

wherein the first surface (150) is made at least partially from a semipermeable membrane (112), and the semipermeable membrane (112) forms a wall of a semipermeable portion (111) of the hollow conduit (110), and

wherein the first surface (150) and the second surface (160) of the probe deviate from being planar, and the curvatures of the first surface (150) and the second surface (160) of the probe (100) are essentially concentric,

wherein the probe (100) is configured to be fixed permanently or non-permanently to a portion (230) of an inner surface (220) of a wall (210) of a reactor (200) with the second surface (160) of the probe (100) facing the portion (230), and preferably wherein the probe (100) is as defined herein.

Yet another aspect of the disclosure is the use of the probe according to the disclosure for measuring and/or monitoring the chemical composition of a fluid medium in a reactor, wherein the probe is fixed permanently or non-permanently to a portion of an inner surface of a wall of a reactor with the second surface of the probe facing the portion to which the probe is fixed, thereby reducing disturbances in the fluid dynamics of the fluid medium in the reactor.

Furthermore, an object of the present disclosure is a method for measuring and/or monitoring the chemical composition of a fluid medium comprising the steps:

a) providing an apparatus as described herein;

b) introducing a fluid medium into the reactor of the apparatus, thus that the first surface of the at least one probe exposed to the interior volume of the reactor is immersed in the fluid medium,

c) optionally agitating, preferably stirring the fluid medium;

d) feeding a perfusion fluid into the hollow conduit through the inlet opening at a predetermined rate;

e) analyzing the chemical composition of the sample fluid released from the outlet opening at predetermined intervals, preferably by chromatographic means, more preferably by high performance liquid chromatography,

wherein the semipermeable membrane is configured to permit diffusion of at least one component, preferably selected from proteins, enzymes, minerals and fatty acids, of the fluid medium and/or the perfusion fluid between the fluid medium in the reactor and the perfusion fluid in the hollow conduit, thus generating the sample fluid in the hollow conduit, and wherein preferably the chemical composition of the perfusion fluid fed into the hollow conduit through the inlet opening corresponds essentially to the initial chemical composition of the fluid medium as introduced into the reactor.

Detailed Description

The invention and embodiments thereof are illustrated in more detail in the following.

A fluid medium in the context of the present invention is not particularly limited and may be any fluid comprising at least one component that is capable of passing through a semipermeable membrane. Preferably, the fluid medium is an aqueous solution, more preferably an aqueous cell culture medium or nutrient solution, more preferably an aqueous nutrient solution, preferably comprising at least one component selected from proteins, enzymes, minerals and fatty acids.

The reactor type used in the present invention is not particularly limited, and may be any type of reactor, preferably bioreactor, known in the art, which can accommodate fluid media, provided that it allows permanent or non-permanent fixture of a probe as described herein to a portion of an inner surface of a wall of the reactor. Preferably, the reactor is suitable for carrying out chemical, biochemical and/or biological processes. More preferably, the reactor is a bioreactor suitable for growing and/or cultivating cell tissue, in particular edible cell tissue.

For example, the reactor may be a container or vessel, such as a bottle, a flask, a vial or a tank, configured to contain a fluid medium, or a conduit, such as a hollow structural section, a tube, a pipe or a hose, through which a fluid medium is passed. Preferably, the reactor is a container or vessel.